

Amendments to the Specification:

Please replace paragraph [0668] of the published application, with the following amended paragraph:

Error-prone frequency was regulated by changing the proofreading function of DNA polymerase δ or ϵ . The proofreading function was changed by producing disparity mutant strains which had a deletion in the proofreading portion of DNA polymerase δ or ϵ . To produce mutant strains, site-directed mutagenesis was used to perform base substitutions at a specific site of DNA polymerases pol δ or pol ϵ of the normal strain (Morrison A. & Sugino A., Mol. Gen. Genet. (1994) 242: 289-296) using common techniques (Sambrook et al., Molecular Cloning: A Laboratory Manual, Ver. 2, Cold Spring Harbor Laboratory (Cold Spring Harbor, N.Y., 1989), supra). Specifically, conversion was performed in pol δ ~~322~~ 321(D) \rightarrow (A); and ~~324~~ 323(E) \rightarrow (A); and in pol ϵ ~~294~~ 290(D) \rightarrow (A); and ~~293~~ 292(E) \rightarrow (A). These mutants were a DNA polymerase δ mutant strain (AMY128-1: Pol3-01 MAT α , ura3-52 leu2-1 lys1-1 ade2-1 his1-7 hom3-10 trp-289 canR; available from Prof. Sugino (Osaka University) and a DNA polymerase ϵ mutant strain (AMY2-6: pol2-4 MAT α , ura3-52 leu2-1 lys1-1 ade2-6 his1-7 hom3-10 try1-289 canR; available from Prof. Sugino (Osaka University). It will be understood that equivalents of such strains can be produced by those skilled in the art using site directed mutagenesis to introduce mutations, such as ~~322~~ 321(D) \rightarrow (A) and ~~324~~ 323(E) \rightarrow (A) in pol δ ; and ~~294~~ 290(D) \rightarrow (A) and ~~293~~ 292(E) \rightarrow (A) in pol ϵ .

Please replace paragraph [0727] of the published application with the following paragraph:

For Pol mutations, one-base mutation was introduced into the proofreading activity sites (SEQ ID Nos. 55 and 56 (δ); SEQ ID Nos. 57 and 58(ϵ)) of both pol δ and pol ϵ to delete proofreading activity: in pol δ 315 314(D) \rightarrow (A), 317 316(E) \rightarrow (A); and in pol ϵ 275(D) \rightarrow (A), 277(E) \rightarrow (A) (Morrison A. & Sugino A., Mol. Gen. Genet. 242: 289-296, 1994; Goldsby R.E., et al., Proc. Natl. Acad. Sci. USA, 99: 15560-15565, 2002).

Please replace paragraph [0745] of the published application, with the following paragraph:

Next similar experiments were carried out using rats as models. Rat models of cancer can be rapidly prepared by introducing mutations into pol δ (in an amino acid sequence as set forth in SEQ ID NO. 60, D at position 315 312 and E at position 317 314 are substituted with alanine).